

Serial No.: 09/745,965  
Attorney Docket: 3373.1

## REMARKS

### *Objection to the Specification*

The Examiner has objected to the disclosure, requiring status updates of all US applications referred to by serial number in the specification. Applicants have amended pages 7, 9, 12, 14, 15 and 22 of the Specification to overcome this objection.

The Examiner has further objected to the Specification because it contains embedded hyperlinks and/or other forms of browser-executable code. Applicants have deleted the embedded hyperlinks from pages 17, 19 and 24 of the Specification to address this objection.

For the above reasons, Applicants respectfully request that the objections to the specification be obviated.

### *Claim Objections*

Claims 3, 12 and 21 are objected to under 37 CFR 1.7(C). For the purpose of expediting the issuance of other claims, Claims 3, 12 and 21 are canceled. Therefore, this objection of claims is obviated.

### *Rejections under 35 U.S.C. § 112*

Claims 1-27 are rejected under 35 USC 112, second paragraph as allegedly containing subject matter which is not enabled. Applicant respectfully disagrees and submits that the claims are fully enabled. Claims 3, 12 and 21 are canceled for the purpose of expediting the issuance of other claims.

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Claims 1-2, 4-11, 13-20, and 20-27 are directed to a method of selecting nucleic acid probes against a target using adjusted quality score which is based upon the quality score and overlapping of the selected probes. As taught in the specification, e.g., pages 30-36, "[i]n selecting multiple nucleic acid probes for one target, one complication that arises is that probes that are nearby each other are mostly redundant. The amount of new data observed from a probe that overlaps with another probe by 24 bases out 25 is minimal." The claimed methods provide a computational approach to balance between the quality scores and the additional information content of probes.

The Examiner states that "[i]n these claims, there is no indication that any of the probes are related to the target sequence in any way. There is no discrete comparison step. One must already have in hand the 'quality score' for a plurality of probes" [page 3, paper no 4]. Applicant respectfully points out that the claimed methods treat quality scores as an input. The methods are applicable to any quality scores as long as the values reflect the desired properties of a single probe. The claims do not recite obtaining quality scores. Rather, it recites inputting quality scores. The quality scores, as defined in the specification (e.g., page 21), are "any qualitative and quantitative values with regard to desired properties of a probe." The specification provides extensive teachings about how one of skill in the art could calculate quality scores based upon sequence information. In addition, a number of patent applications that teach the calculation of quality scores are incorporated by reference. Applicant respectfully submits that various methods for calculating quality scores are well known in the art. For example, the Examiner has identified a reference (Mei and Hardin, et al., 2000) which provides another example of how one can obtain qualitative and quantitative values with regard to desired properties of a probe.

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The Examiner also alleges that "the claims further lack steps which set forth how the actual or predicted quality scores are used to obtain the "maximum aggregate adjust quality score" and "The specification sets forth only a single method for adjusting scores and one of skill in the art would not be able to easily determine what other ways to base such an adjustment without undue experimentation." Applicant respectfully disagrees and submits that the claim recites that the quality scores are adjusted according to the overlap between probes. The specification teaches in great detail how to adjust quality scores to account for information content. For example, at page 30, several exemplary rules are provided. These rules specify the details of how the adjustment is made. Methods for implementing these rules are well within the ordinary skill in the art and do not require undue experimentation. At page 31, a specific example is provided.

The Examiner also alleges "performing dynamic programming optimization fails to remedy the preceding problems. On what is this to be done? To what end?" Applicant respectfully submits that dynamic programming optimization is well known in the art. With regard to what is this to be done and to what end, the specification clearly teaches that "optimization methods are used to pick an optimal set of  $k$  probes from  $n$  probes provided with initial scores and locations of the probes in the target sequence." [page 31] A specific example (Figure 15) and computer codes are also provided. The specification also explains detailed process of an exemplary dynamic programming optimization.

For the reasons above, Applicant respectfully submits that the specification provides detailed teachings about how to adjust quality score for information content and the dynamic programming optimization process. The claims are enabled to its full scope. Therefore, this rejection of claims under 35 USC 112 should be withdrawn.

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***Rejections under 35 U.S.C. § 102***

Claims 1, 39 and 77 are rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Mei et al. (2000). Applicant respectfully disagrees.

The rejected claims are directed to adjusting quality scores for overlap of probes. In contrast, Mei et al. discusses a primer selection program for octamer sequencing technology. The reference does NOT disclose selection of "desired number of probes from a library of probes based upon their length, overlap with other probes in the library and predicted affinity for target sequences." In fact, the primer selected is octamer. The final selection is based upon the  $\Delta G$  and the secondary structure of the template. Because the cited reference does not disclose adjusting quality score for overlap of probes, Applicant respectfully requests that the claim rejections under 35 U.S.C. § 102 should be withdrawn.

**CONCLUSION**

For these reasons, Applicants believe the application is now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5000.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

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If the Examiner has any questions pertaining to this application, the Examiner is requested to contact the undersigned attorney.

Respectfully submitted,



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